

## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant	:	Mishra, Allan	)	Group Art Unit: 1645
			)	
Appl. No.	:	10/581,577	)	
			)	
Filed	:	June 2, 2006	)	
			)	
For	:	<b>METHOD OF TREATING</b>	)	
		<b>CANCER USING PLATELET</b>	)	
		<b>RELEASATE</b>	)	
Examiner	:	Khatol Shahnan Shah		

DECLARATION UNDER 37 C.F.R. § 1.132

Assistant Commissioner for Patents  
Washington, D.C. 20231

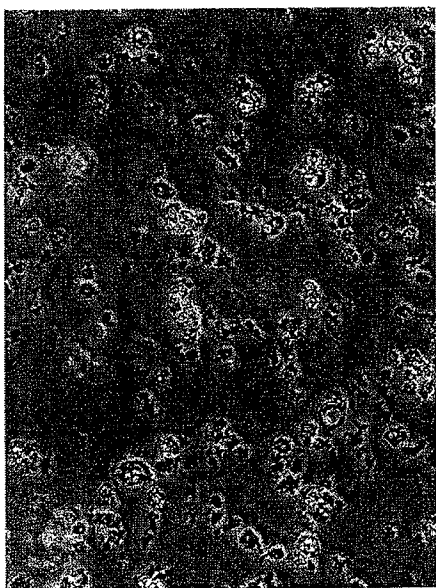
Dear Sir:

I, Allan Mishra, declare as follows

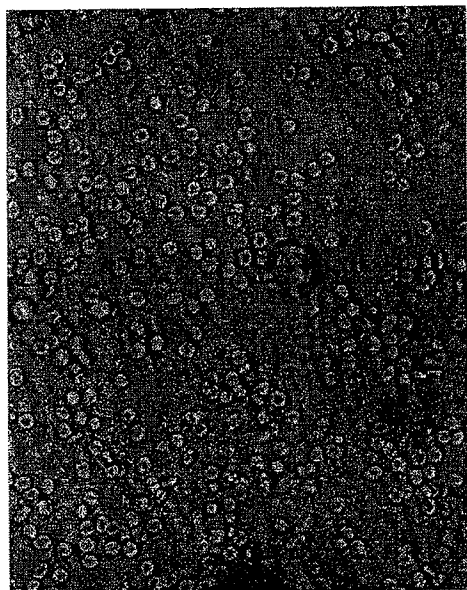
1. I am the inventor of the above-identified application. My curriculum vitae is attached hereto.
2. The following experiment was done by myself or under my supervision. PRP was prepared from whole blood and then exposed to energy waves to break open the platelets and obtain the platelet releasate. The energy waves were ultrasonic and were applied for 8 seconds. Human glioblastoma cancer cells were grown in cell culture in control media and 10% buffered using platelet rich plasma (PRP) for 10 days. The PRP was buffered using sodium bicarbonate to physiologic pH, around 7.4.
3. No exogenous activator was used. Specifically, no thrombin, calcium or epinephrine was added to the PRP or cultures.
4. At 10 days after incubation with PRP, photomicrographs were taken to analyze the morphologic characteristics of the cancer cells. At that time, marked differences in the structure of the cells were clear under microscopic examination. Differentiation into more normal cells, possibly astrocytes, was observed. See figures 1-3.

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**Figure 1: No PRP, Lack of cell differentiation, cancer-like morphology**

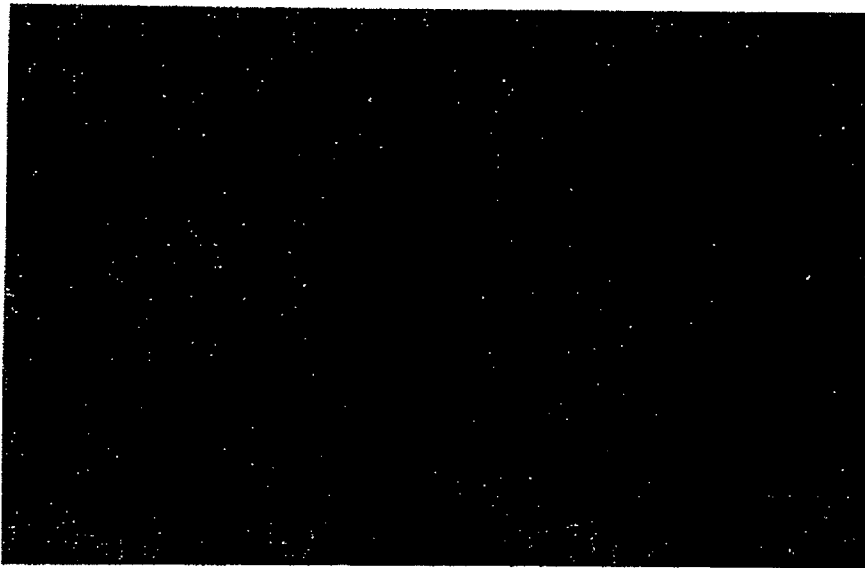


**Figure 2: 10% PRP, Cell differentiation, more normal morphology**



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**Figure 3: PRP 10%, Cell Differentiation, possibly into an astrocyte**



5. I declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful, false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States codes and that such willful, false statements may jeopardize the validity of the application or patent issuing therefrom.

Dated: \_\_\_\_\_

8/28/09

By: \_\_\_\_\_

Allan Mishra, MD



**ALLAN K. MISHRA, MD**

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Menlo Park, CA 94025**

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**Present Positions:**                    **Adj. Clinical Assistant Professor  
Stanford University Department of Orthopedic Surgery**

**EDUCATION, MEMBERSHIPS, AND ASSOCIATIONS**

**Fellow:**                                    **American Academy of Orthopaedic Surgery (AAOS)**

**Diplomate:**                              **American Board of Orthopaedic Surgery (Board Certified, 1997, Recertified 2006)**

**AAOS**                                        **National Membership Committee, 2006-  
Candidate Member Committee, 1998-2005  
Instructional Course Lecturer, 1998-2009**

**President/Founder:**                    **Biologic Orthopedic Society, 2009**

**Associate Team Physician:** **USA Decathlon Team, 1996**  
• Participated in the Atlanta Olympics Medical Team

**Doctor of Medicine:**                   **The University of Michigan Medical School, June 1989**  
• President, Galens Medical Society

**Bachelor of Science:**                   **The University of Michigan, May 1986**  
• Accelerated Premedical-Medical Program, Inteflex  
• Golden Key Honor Society

**POST GRADUATE TRAINING**

**Fellowship:**                              **Sports Medicine  
Stanford University Medical Center; Palo Alto, California**

**Residency:**                              **Orthopaedic Surgery  
Beaumont Hospital; Royal Oak, Michigan, 1990-1994**

**Internship:**                              **General Surgery  
Beaumont Hospital; Royal Oak, Michigan, 1989-1990**

## **PEER REVIEWED PUBLICATIONS**

**"Buffered Platelet Rich Plasma Enhances Mesenchymal Stem Cell Proliferation and Chondrogenic Differentiation"**

Tissue Eng Part C Methods. 2009 Feb 13

**"Point-Counterpoint: Platelet Rich Plasma Compared with Cortisone Injection for Chronic Lateral Elbow Tendinosis"**

Archives of Physical Medicine and Rehabilitation, April 2009

**"Treatment of Tendon and Muscle with Platelet Rich Plasma"**

Clin Sports Med. 2009 Jan;28(1):113-25.

**"Cellular effects of platelet rich plasma: Interleukin-1 Release from PRP Treated Macrophages."**

Biomed Sci Instrum. 2008;44:489-94

**"Selecting and Starting an Orthopaedic Surgery Practice"**

Instructional Course Lectures Volume 57

AAOS Instructional Course Lectures 2008

**"Cellular Effects of Platelet Rich Plasma: A Study of HL-60 Macrophage-Like Cells"**

Biomed Sci Instrum. 2007;42:266-71

**"Treatment of Severe Elbow Epicondylar Tendinosis with Buffered Platelet Rich Plasma"**

American Journal of Sports Medicine, Nov. 2006

Presented at the 2005 AAOS Washington, DC and Internationally in Spain, Italy, England and Sweden

**"Compartment Syndrome Resulting from the Use of an Electronic Cooling Unit"**

American Journal of Sports Medicine, September 2004

**"Elbow Rehabilitation in Athletes"**

A chapter in: Surgery of the Elbow--Practical and Scientific Aspects, 1997

**"A Symptomatic Cyamella Simulating a Lateral Meniscus Tear"**

The Journal of Arthroscopic & Related Surgery, June, 1996

**"Maintenance of Aerobic Capacity During Recovery from right foot Jones Fracture"**

Clinical Journal of Sports Medicine, 1996

**"Arthroscopy"**

A chapter published in: Kelly's Textbook of Internal Medicine, 1996

**"Graft Harvesting via Horizontal Incisions"**

The Journal of Arthroscopic & Related Surgery, Vol. 11, No 6 December, 1995

**"The Cutaneous and Radiologic Manifestations of Musculoskeletal Disease"**

Resident and Staff Physician; 12:37:17-28, 1991

## **FEDERAL PRESENTATIONS**

### **“Basic Science and Clinical Experience with Platelet Rich Plasma”**

Presentation to the Food and Drug Administration (FDA)  
Washington DC, Dec. 2007

### **“Platelet Rich Plasma, an Emerging Biologic Tool”**

Presentation to the Centers for Medicare and Medicaid Services (CMS)  
Washington, DC, 2006

## **ACADEMIC PRESENTATIONS**

### **“Platelet Rich Plasma Round Table”**

Orthopedics Today March 2009

### **“Choosing an Orthopedic Practice”**

AAOS Instructional Course Lecture  
Las Vegas, NV, Feb. 2009

### **“Point of Care Regenerative Medicine Using PRP”**

BioBridge Regenerative Medicine Conference  
Geneva Switzerland, September 2008

### **“Pioneering the Use of Platelet Rich Plasma”**

Trends in Tendinopathy  
Netherlands, June 2008

### **“Selecting and Starting an Orthopedic Surgery Practice**

AAOS Instructional Course Lecture  
San Francisco, CA March 2008

### **“Application of Growth Factors for Tendinopathy”**

International Meeting of Sports Medicine  
Chamonix, France; Jan. 2008

### **“AAOS Fellow Takes European “PRP Tour”**

AAOS Now, Jan. 2008

### **“In Vitro and In Vivo Uses of Platelet Rich Plasma”**

Invited lectures in Stockholm, Sweden and Genoa, Italy September 2007

### **“Orthopedic Applications of Platelet Rich Plasma”**

Peninsula Equine Summer Symposium in conjunction with the International Society of Equine Locomotor Pathology, August 2007

### **“Buffered Platelet Rich Plasma Enhances Mesenchymal Stem Cell Proliferation and Chondrogenic Differentiation”**

2007 AAOS Meeting San Diego, CA

### **“Research and Clinical Applications of Platelet Rich Plasma”**

Presented in various European meetings in Milan, Italy; Barcelona, Spain and England; May 2006

## **ACADEMIC PRESENTATIONS**

### **"Human Fibroblast Proliferation in Platelet Rich Plasma"**

2006 AAOS Meeting, Chicago, IL

### **"Use of PRP in Orthopedic Surgery"**

Invited lectures in Amsterdam, Netherlands and Barcelona Spain  
June 2005

### **"Treatment of Chronic Elbow Tendinosis with Platelet Rich Plasma"**

2005, AAOS Meeting, Washington, DC

### **"How to Choose an Orthopedic Surgery Practice"**

Presented as part of an Instructional Course Lecture, AAOS Annual Meeting, Feb. 2003

### **"Musculoskeletal Medicine Update"**

A CME Course for primary care providers  
Stanford University Medical Center, 2002-2003

### **"Practice Management Skills"**

Young Orthopedists Forum Presentation, AAOS Annual Meeting, Feb. 2002

### **"Stanford Shoulder Score"**

A Predictor of Shoulder Trauma Diagnosis and Outcome, Presented June 2001, Stanford Research Day

### **"Emerging Information Technology"**

Presented as part of an Instructional Course Lecture, AAOS Annual Meeting, March 2001

### **"The Internet and the Practice of Orthopedic Surgery"**

Presented as part of an Instructional Course Lecture, AAOS Annual Meeting, April 2000

### **"Managed Care for Young Orthopedists"**

Presented at the AAOS Annual Meeting Feb. 1999

### **"Malnutrition--An Accurate Predictor of Morbidity, Mortality and Hospital Cost in Elderly Hip Fracture Patients"**

Presented at AOA Resident's Meeting, March 1993 and the Mid-America Orthopaedic Association Meeting, April 1993; ■Phemister Award for excellence

### **"The Sensitivity and Specificity of TC-99M/Sulfur Colloid and Indium-111 WBC Imaging in Detecting an Infected Hip Arthroplasty"**

Presented at AOA Resident's Meeting, March 1992 and the Mid-America Orthopaedic Association Meeting, April 1992; ■First Place Winner, Detroit Orthopaedic Association Residents Papers Conference, May 1992

### **"Cardiac Hypertrophy and Cardiomyopathy in Pheochromocytoma"**

Poster Presentation, FASEB; April 1986

## **CURRENT RESEARCH PROJECTS AND INTERESTS**

**Biologic Treatments for Tendon, Cartilage and Spinal Disorders**

## **OTHER RESEARCH EXPERIENCE**

<b>Grants Raised</b>	Biomet Unrestricted Educational Research Grant: 2002 Depuy Unrestricted Educational Research Grant: 2003
<b>Journal of Orthopedic Research</b>	Manuscript Editor and Reviewer: 2008—
<b>Journal of Cellular and Molecular Medicine</b>	Manuscript Editor and Reviewer: 2008—
<b>Annals, Academy of Medicine, Singapore</b>	Manuscript Editor and Reviewer: 2009—
<b>Wilderness Medical Journal</b>	Manuscript Editor and Reviewer: 2003—
<b>Clinical Journal of Sport Medicine:</b>	Associate Editor, Journal Club; 1994-2001
<b>Stanford University Medical School:</b>	Research Assistant, 1985 Responsible for cardiac surgical procedures and analysis
<b>The University of Michigan Medical School:</b>	Research Assistant, 1984-1985 Collaborated on a variety of projects Responsible for Canine Open Heart Surgery

## **CERTIFICATIONS**

<b>Fellow</b>	American Academy of Orthopedic Surgery
<b>Board Certified</b>	American Board of Orthopedic Surgery
<b>Diplomat:</b>	National Board of Medical Examiners
<b>Physician License:</b>	State of California

## **OTHER AFFILIATIONS AND ACTIVITIES**

<b>PGA Physician:</b>	ATT-Pebble Beach Pro-Am Golf Tournament, 2001-2004 First Tee Champions Tournament, 2004
<b>Guest Disc Jockey:</b>	KITS, San Francisco and WCSX, Detroit
<b>Interests:</b>	Skiing, triathlon training and No-Limit Poker